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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,588	01/21/2004	Grigoriy S. Tchaga	CLON-056US2	3721
24353	7590	08/10/2006	EXAMINER	
BOZICEVIC, FIELD & FRANCIS LLP 1900 UNIVERSITY AVENUE SUITE 200 EAST PALO ALTO, CA 94303			ROOKE, AGNES BEATA	
			ART UNIT	PAPER NUMBER
			1653	

DATE MAILED: 08/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/762,588

Applicant(s)

TCHAGA ET AL.

Examiner

Agnes B. Rooke

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 07 June 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 11-13, 16, 18-21, 23, and 24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11-13, 16, 18-21, 23, 24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

This final office action is in response to the paper filed on 06/07/2006.

Claims 11-13, 16, 18-21, and 23-24 are pending and currently under examination. Claims 1-10, 14-15, 17, and 22 are cancelled.

***Double Patenting rejection is withdrawn in view of the Terminal Disclaimer submitted on 06.07/2006.***

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 11-13, 16, 18-21, and 23-24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Tchaga et al. WO 99/57992 in view of by Porath et al., "Immobilized Metal Ion Affinity Adsorption and Immobilized Metal Ion Affinity Chromatography of Biomaterials. Serum Protein Affinities for Gel-Immobilized Iron and Nickel Ions," Biochemistry (1983), 22, p. 1621-1630.

Tchaga et al. teach the instant SEQ ID NO:1 in the sequence listing section on page SEQ 7/7, as SEQ ID NO:6. (claims 11, 18, 23, and 24).

Figures 1, 2, and 3 depict the vectors with different restriction sites; and on pages 19 and 20 of the specification the invention teaches recombinant vector comprising

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DNA sequence where the recombinant vector is capable of directing expression of said DNA sequence for the fusion protein; see claims 1, 2, 6-9 of Tchaga et al.

Further, on page 9 lines 21-24 of the specification, metals that can be used for purification or immobilization of fusion proteins are disclosed and include, Ni(II), Co(II), Zn(II), Cu(II), Ac(III) and Fe(III).

Further, Tchaga et al. teaches different buffers that can be used in the purification of proteins, see Example 4, pages 14 and 15.

Tchaga et al. do not teach two different column/resin that are used in the purification.

Porath et al. teach metal chelate affinity chromatography for purification of serum proteins, where gels are loaded with the same or different metal ion, for example Ni(II) and Fe(III). See *Abstract*.

Porath et al. prepared different columns, for example "IDA-Sepharose 6B" or "TED-Sepharose 4 B" with bound Ni(II) or bound Fe(III), where each chelator gel was packed in a separate column. See page 1622 (*Materials and Methods* section). Different combinations of columns were formed, where two or more columns were packed with one type of chelator gel (e.g., TED-Sepharose) and loaded with different metal ions (e.g., Ni(II) or Fe(III)) to form "tandem columns". See page 1622 (*Chromatography* section). Different combinations of "tandem columns" were created where Fe(III)-TED bed preceded Ni(II)-TED or Ni(II)-TED bed preceded Fe(III)-TED bed. See page 1624 (*Results* section). The following buffers were used for extraction, wash, and elution

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purposes: 0.05M sodium acetate and 0.1 M NaCl, pH 5.5; 0.1 M Tris-HCl, pH 8.1; 0.5 M sodium acetate, pH 5.5; and 1M glycine, pH 9.0 (Claims 11 and 16).

Therefore, it would have been obvious to one skilled in the art at the time invention was made to design different resins as taught by Porath et al. and include in the design a vector as taught by Tchaga et al. because these kind of designs of columns for purification of proteins are known and commonly used in the art in the art.

Applicants responded that Tchaga et al. disclose addition of the ion affinity peptide which efficiently complexes metal ions as the mechanism of increased specificity and adsorption affinity, as it prevents the participation of the native protein in adsorption; and that one skilled in the art finds no motivation to improve upon such a protocol, nor any suggestion that the use of a second column or a different metal ion would be a means to do so.

Examiner responds that it is irrelevant whether the protein is native or non-native, since either of them can be used in the protocol. Further, purification of proteins usually occurs in the presence of different columns (depending on the desired percent recovery of a protein), and the use additional columns (in tandem, for example) or different ions in the protocol is dictated by the need to optimize the conditions for most efficient and maximum recovery of the protein of interest. Therefore, Tchaga et al. still applies.

Next, Applicants state that Porath et al. describe the use of columns packed with agarose chelator gels loaded with different metal ions linked in tandem in order to

separate untagged serum proteins, where here the absorption is mediated entirely by the native protein by a mechanism which is poorly understood.

Examiner responds that it is irrelevant that Porath et al. refers to untagged proteins, since the idea is to use metal ion affinity chromatography to purify a protein of interest.

Moreover, Applicants state that the affinities of specific metal ions for specific features of the bound protein are broadly theorized but are not known, and that in Porath et al. the rationale for using multiple metal ions stems from the need to vary the specificity of adsorption of different protein components of the sample where the goal is to maximize specificity and not high-efficiency recovery.

Examiner responds that maximizing specificity and high-efficiency recovery go hand in hand in protein purification since, maximum specificity can cause high-efficiency of recovery, as it is desired when using any purification kit.

Further, Applicants state that the suggestion to combine the cited references is absent from the references themselves, neither reference describing nor suggesting the assembly of kits for purifying a protein with both a first and second metal ion chelate resin in combination with a recombinant vector which facilitates the fusion of a heterologous molecule to a metal ion affinity peptide as presently claimed.

Examiner respectfully disagrees and maintains the position that there is a clear motivation to combine the teachings of Tchaga et al. and Porath et al. because Tchaga et al. teach SEQ ID NO:1, expression vectors, and different metals (Ni, Co, Zn, Cu, Ac, and Fe) and buffers that can be used for purification or immobilization of fusion proteins.

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Then, Porath et al. teach metal chelate affinity chromatography for purification of proteins, where the gels are loaded with the same of different metal ion (Ni, Fe); where each chelator gel is packed in a separate column; where different combinations of columns are formed and loaded with different metal ions (Ni, Fe).

Therefore, it would have been obvious to one skilled in the art at the time invention was made to design a kit with different resins as taught by Porath et al. and include in the design an expression vector, and SEQ ID NO:1 as a metal ion affinity peptide, as taught by Tchaga et al., because the proteins of Porath et al. can be substituted with SEQ ID NO:1 of Tchaga et al. to achieve the same goal of protein purifications using metal ion affinity chromatography.

One would be motivated to design such kits that include a vector, SEQ ID NO:1, and a different combination of metal chelate resins for purifying a protein of interest, since such designs are very efficient and already used in the prior art. Therefore, the rejection stands.

### ***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not


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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-273-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

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ROBERT A. WAX  
PRIMARY EXAMINER